

Claims 1-10 stand rejected under 35 U.S.C. §112 (second paragraph) as being indefinite.

Claims 1-3 and 6-10 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Gathiram et al. *Circulatory Shock*, 27 pp 103-109 (1989) in view of Theofan et al., U.S. 5,420,019 and Boermeester et al. *Intensive Care Medicine*, 20 (suppl 1), p. s122, abstract 478, March 1994.

Claims 1, 4 and 5 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Gathiram et al. *Circulatory Shock*, 27 pp 103-109 (1989) in view of Theofan et al., U.S. 5,420,019; Boermeester et al. *Intensive Care Medicine*, 20 (suppl 1), p. s122, abstract 478, March 1994; and Caty *Annals of Surgery* 212(6):694-700 (1990).

Claims 1-10 stand rejected over claims 1-8 of U.S. 5,578,568 for obviousness-type double patenting.

Claims 1-10 stand rejected over claims 1-8 of U.S. 6,017,881 for obviousness-type double patenting.

III. Patentability Arguments

The rejections should be withdrawn and claims 1-5 and 8-10 should be allowed for the reasons set out below.

A. The Rejection of the Claims Under 35 U.S.C. §112 (first and second paragraphs) Should be Withdrawn.

The rejection of claims 1-10 under 35 U.S.C. §112 (first and second paragraphs) should be withdrawn in light of the amendments to claim 1 to recite treatment of cardiac arrhythmias as acknowledged by the Examiner to be enabled and to specifically recite the full

name of bactericidal/permeability-increasing protein (BPI). Applicants have fully supported the recitation of "BPI protein product" in their specification teaching a wide variety of biologically active analogs and variants of BPI which are the subject of co-owned U.S. patents and applications the disclosures of which were incorporated by reference in the specification. As evidence thereof, Applicants point out that both the parent and grandparent patents of the present application (U.S. 5,578,568 and U.S. 6,017,881) respectively recite "BPI protein product" in their claims.

Further, claim 1 has also been amended to recite a process step referring to the claim preamble as requested by the Examiner. Finally, claim 1 was amended to recite the result of reducing the duration of cardiac arrhythmia as disclosed in the specification at page 9, lines 20-25 and Figure 6. Accordingly, the rejections under 35 U.S.C. §112 (first and second paragraphs) should be withdrawn.

B. The Rejections Under 35 U.S.C. §103(a) Should be Withdrawn.

The rejections under 35 U.S.C. §103(a) should be withdrawn because there is no teaching in the art of an association of cardiac arrhythmia with sepsis. Specifically, reference is made to the Declaration of Dr. William Steve Ammons submitted with the Response dated August 24, 1995 in grandparent U.S. Application Serial No. 08/232,527 which issued as U.S. Patent No. 5,578,568. In that Declaration (Attached hereto as Appendix A) referring in part to the disclosures of Bone "Gram-Negative Sepsis Background, Clinical features, and Intervention" *Chest*, 100: 802-808 (September 1991) Dr. Ammons stated the following at paragraphs 8 and 9:

8. That the adverse physiological effects of bradycardia, respiratory depression and arrhythmias, described in Example 1 of the patent application as associated with intestinal ischemia/reperfusion, are not adverse effects of sepsis. In fact, the opposite effects of tachycardia and increased respiration are associated with sepsis (see, e.g., review of Gram-Negative Sepsis by Bone, attached as Appendix 26 to this Declaration).

9. That the effects of BPI, as demonstrated in Example 1 of the patent application, on bradycardia, respiratory depression, arrhythmias and hypotension were unexpected, and particularly surprising was BPI's effect on arrhythmias in intestinal ischemia/reperfusion.

Thus, the rejections under 35 U.S.C. §103(a) should be withdrawn because the cited art fails to disclose or suggest using BPI to treat the adverse physiological effect of intestinal ischemia/reperfusion which is cardiac arrhythmia.

C. The Obviousness-type Double Patenting Rejections Should be Withdrawn in Light of the Terminal Disclaimer Submitted Herewith.

The rejections of claims 1-10 under the doctrine of obviousness type double patenting over claims 1-8 of U.S. Patent No. 5,578,568 and claims 1-11 of U.S. Patent No. 6,017,881 should be withdrawn in light of the Terminal Disclaimer (Exhibit B) and the fee under 37 C.F.R. §1.20(d) submitted herewith.

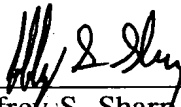
IV. Conclusion

It is submitted that each of claim 1-5 and 8-10 should now be indicated to be allowable. Should the Examiner have any questions of form or substance, he is invited to contact the undersigned attorney as the number listed below.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claims 6 and 7 have been canceled.

Claim 1 has been amended as follows:

1. [AMENDED] A method of treating adverse physiological effects associated with intestinal ischemia/reperfusion wherein the adverse physiological effect is cardiac arrhythmia comprising administering to a subject suffering from the effects of intestinal ischemia/reperfusion an [effective] amount of a bactericidal/permeability-increasing (BPI) protein product effective to reduce the duration of cardiac arrhythmia resulting from intestinal ischemia/reperfusion.